Experimental Results of Poisonous Doses of Quinine and Salicylic Acid Upon the Auditory Apparatus of Animals.—KIRCHNER (*Berliner klin. Wochenschrift*, 1881, No. xci.) claimed that doses of from one to two grammes of quinine and from three to five grammes of salicylate of soda, given to cats, dogs, and guinea-pigs, produced in a few hours hyperæmia and hemorrhages in the middle ears, the internal ears, and fourth ventricle. The large doses of quinine killed cats and dogs in from five to eight hours, death being ushered in with symptoms resembling those of suffocation. The objection was soon raised to his conclusions that the results in the ears, on which they were based, were due to strangulation and not to the poisonous effects of the drugs given the animals.

C. GRUNERT (*Archiv f. Ohrenh.*, November 30, 1898) has recently made some experiments on white mice and pigoens in order to determine whether "suffocation could produce destructive changes in the auditory organ similar to those produced by Kirchner's poisonous doses of quinine, etc."

By these experiments with suffocation Grunert could produce hyperæmia of the auditory organ but not extravasations, whereas Kirchner evoked by his experimental drugs not only great hyperæmia but extensive blood extravasations in the endolymphatic spaces, functionally the most important spaces in the auditory apparatus. Grunert, therefore, believes that the "above-named extravasations of blood in the ductus cochlearis, for example, as produced by Kirchner, must be the result of specific, poisonous action of the drugs, induced, perhaps, through the great injury sustained by the blood-vessels of the tract under consideration."

A practical conclusion drawn by Kirchner and confirmed by Grunert is that if the internal ear is unduly congested by an overdose of quinine or salicylic acid it can never recover its function. [Caution demands the avoidance of large doses at a time to the human being.—ED.]

Acute Otitis Media.—In the acute inflammatory stage of otitis media, GORHAM BACON (*New York Polyclinic*, January 15, 1898) holds that it is important to apply the artificial leech at once, close to the tragus, and endeavor to abort the disease. If the drumhead bulge a free incision should be made into it. This should be done only under the guidance of the eye and with the aid of good illumination. If the free incision is not made and proper drainage not established there would be great danger of the otitis media becoming chronic. If the disease become chronic in the attic, the perforation should be enlarged and the endeavor made to wash out the secretion with a syringe. Granulations should be destroyed by the application of chromic acid or by the use of the curette. If this treatment failed a cure could be effected in many cases by excision of the ossicles and curetting the attic. Some of the results of chronic otitis media are the formation of granulations and polypi, caries of the ossicula and temporal bone, mastoid disease, suppurative meningitis, cerebral abscess, and septicæmia. In cases of acute otitis media, if the temperature remains high after the incision of the drum membrane and the opening of the mastoid cells, one should think of a complicating pneumonia or, perhaps, of a sinus thrombosis. In cases of acute mastoid disease the operation should not be deferred until redness and œdema of the tissues over the mastoid appear and the auricle stands out prominently from the head. In making the diagnosis the two mastoid processes should be compared, as in some persons pressure on an uninflamed mastoid process causes pain. In the first stage of mastoid inflammation, secondary to acute suppurative otitis media, after incision the artificial leech should be applied and also the Leiter cold coil; but the latter should not be left on for more than forty-eight hours, for if the symptoms have not subsided by that time immediate operation is indicated. The incision should be made close to the auricle, from the tip to the upper border of the pinna. This incision can be enlarged in both directions if complications exist. When pus is found in the antrum and upper part of the mastoid it should be remembered that the tip might contain pus, and if this is not liberated it may burrow down into the tissue of the neck and give rise to septicæmia. When caries of the tympanic roof takes place a collection of pus is frequently found in the temporo-sphenoidal lobe.

A. H. Buck (*New York Polyclinic*, January 15, 1898) said with the early stage of acute otitis media one must choose between hot and cold applications. In his opinion, both of these agents are vasomotor stimulants, and they relieve the pain through this vasomotor action by diminishing the pressure on the sensory nerve-fibres of the inflamed part. Heat had no power to benumb sensation, while cold would do so when carried beyond a certain point. This very application of cold, therefore, served to mislead us, for it is largely by the persistence of pain that we are informed of the necessity of going further and operating. The application of ice appeared to be getting very popular in this country, and for this reason he felt called upon to emphasize the fact that it was a very deceptive agent. Robert Abbe (*New York Polyclinic*, January 15, 1898) said that the discussion on Dr. Bacon's paper on "Suppurative Otitis Media and its Complications" had shown most clearly the great risk of allowing a purulent otitis to go on after the onset of serious symptoms. Hemorrhage, sinus pyæmia, and cerebral abscess were the great dangers to be feared. If the mastoid was operated upon quite early the involvement of the sinus would be exceedingly slight. If, however, the operation was deferred, the signs and symptoms of sinus pyæmia would soon make their appearance—tenderness and induration along the jugular vein.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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The Action of Streptococci and of Their Toxins on the Various Organs of the Body.—The whole number of *Ziegler's Beiträge für pathologischen Anatomie*, 1899, Band xxv., Heft 1, is devoted to a study by Homén and his pupils of the effect of one particularly virulent streptococcus and of its toxin on various organs of the body. The toxin was obtained in concentrated form from bouillon cultures by precipitation, either by ammonium sulphate or by amyl alcohol. The results are briefly as follows:

NERVOUS SYSTEM (Homén and Laitinen). A parallel series of experiments was made on rabbits, of which about three hundred were used. Injections either of the streptococcus or of its toxins were made into the right sciatic nerve or into the cord. The clinical symptoms varied greatly and were carefully noted. More or less paralysis of the hind leg was frequent, and in cases that lived a long time atrophy of the leg sometimes occurred.

In animals that died within a week after inoculation in the sciatic nerve with the streptococcus the nerve was usually deeply injected, swollen, and œdematous. In cases that lived longer the lesions were less marked. After injection of the toxin the mascroscopical changes were exceedingly slight.

Microscopical changes were usually found in the nerves, nerve-roots, spinal ganglia, and cord.

In the peripheral branches of the nerve-bundle the bacteria seemed from the beginning to be scattered rather diffusely in the nerve substance; in the proximal portion, however, within a very few centimetres above the point of inoculation, they were collected chiefly in the lymph space on the inner side of the perineurium, from which they penetrated gradually into the centre of the nerve-bundle along the endoneural continuations of the perineural sheath.

In the extension to the cord the organisms seemed to travel more along the posterior nerve-roots. In general they then spread very quickly throughout the intermeningeal spaces of the whole cord, collecting chiefly around the nerve-roots, and penetrated also the corresponding spaces of the brain. They got into the cord, especially along the posterior septum, but also at other points, chiefly along the pial sheaths of the bloodvessels. It is worthy of notice that lesions caused by the bacteria were sometimes localized in the neighborhood of the anterior nerve-roots, especially at the anterior edge of the anterior horns.

A week after the inoculation, sometimes earlier, no bacteria, as a rule, could be found in the cord, but they could sometimes be found as late as the seventeenth day in the injected nerve, usually, however, in a degenerated condition.

The histological lesions were closely associated with the localization of the bacteria. The effect of the bacteria, that is, of their toxins, was a diffuse change resulting in granular degeneration, followed by cellular increase due to immigration of leucocytes, and proliferation of the cells of the endoneurium and of the nerve-sheaths.

On the whole, the bacteria do not penetrate much into the spinal ganglia. The ganglionic cells showed the greatest variations in the degenerative changes of the chromophilic elements. Bacteria and pathological changes were found in general more in the posterior than in the anterior nerve-roots.

The most noticeable lesions in the cord after injection of bacteria into the nerves were the localized changes at those places where the bacteria were also sometimes found, and also the changes in the cells of the anterior horns.

It is remarkable that the distribution of the bacteria and of the lesions was practically the same, whether the injection had been made into the nerves or into the cord.

After injections of the toxins the changes on the whole were the same whether the injection was made into the cord or into the nerve.

The changes in general, as well after the injection of the bacteria as of toxin, were at first more of a degenerative nature, and were followed by inflammatory and sclerotic processes; at times the process from the beginning was more of an exudative nature.

Aside from the small differences in the histological changes and in their distribution, the lesions which occurred after injection of bacteria or of the toxin were in general so alike that it must be assumed that the chief paths of distribution of the bacteria and of the toxin are essentially the same, and that the bacteria produce their effect chiefly through their toxin.

The writers are of the opinion that their investigations to some extent favor the view that many affections of the cord—not only those of a more degenerative but those of an inflammatory character—are of an infectious or toxic nature. They believe that their work furnishes an anatomical foundation for the theory of ascending neuritis.

LIVER. BJÖRKSTÉN presents a series of cases showing the action of streptococci and their toxins in the liver.

He injected the liver in five different ways: directly into the liver, into a vein, subcutaneously, into the sciatic nerve, and by introducing a glass tube into the common bile-duct.

In order to infect the common bile-duct thoroughly a laparotomy was performed, with complete aseptic precautions, the duodenum opened, a small sterile glass tube introduced into the bile-duct, the duodenum closed, and the tube broken.

In direct injection into the liver most cases died of peritonitis and general infection. Those which did not die were killed at 1, 4, 10, 30, and 60 days after the infection.

In most of the cases there was a rise of temperature lasting from three to ten days, and considerable loss of weight.

After injection of the streptococci he found that in the cases of general infection, independent of the methods of injection, streptococci were found in the liver in those dying early, but not in those dying after the thirteenth day; they were between the liver-cells or in the capillaries; the parenchymatous cells near the clumps of bacteria, within a few days after the infection, were very often changed; round-cell infiltration and necrotic areas often occurred, and sometimes hemorrhages irrespective of these areas. The liver could be infected with streptococci through the common bile-duct without marked general infection. The streptococci in those cases so infected and examined within thirteen days could be found in and about the bile-passages, together with small-cell infiltration and often degenerative changes in the surrounding parenchyma cells.

After injection of the streptococcus toxin the general condition of the animal was impaired; there was a rise of temperature, and then the animal recovered or grew worse, according to the method of infection. Direct injection caused marked degenerative changes in the tissue.

Injection of the toxin through the common bile-duct caused degeneration and breaking up of the parenchyma surrounding the bile-passages. A loose and swollen connective tissue was formed, in the meshes of which fragments of broken-down liver-cells were often seen. There were also many round-cells and marked increase of the connective tissue cells, especially in the region near the bile-ducts. The meshes of the connective tissue stroma became gradually smaller and finally disappeared, so that a complete cirrhosis might result. Small areas of degeneration or necrosis could be caused by the injection of the toxin into the sciatic nerve or into a vein.

LUNGS. SILFVAST found that streptococci introduced into the lungs of rabbits were immediately taken up in large numbers by the epithelial cells. Fifteen minutes after the intratracheal injection of a bouillon culture numerous alveolar epithelial cells were studded with streptococci. The polymorphonuclear and large mononuclear leucocytes were less phagocytic. After the first four hours more extracellular cocci were seen, and they appeared better preserved. After the second day the micro-organisms began to degenerate, and by the twelfth day cultures from the lung were sterile.

Streptococci were found in the bronchial lymph-nodes fifteen minutes after the introduction of the organisms into the trachea. They were also demonstrable thirty-five days later.

The lungs of the rabbit were quite resistant to the action of the streptococcus. Exposure of the animal to a low temperature, or a local cooling of half the thorax, had a remarkable effect in diminishing this resistance. The inhalation of a mechanical irritant, such as powdered charcoal, had a similar predisposing action.

Both living streptococci and their toxins caused diffuse and focal changes. The pathological process began with the emigration of polymorphonuclear leucocytes, the desquamation of alveolar epithelium, and the exudation of a coagulable fluid. Later there was a diffuse infiltration consisting of various kinds of leucocytes, swollen epithelial cells, red blood-corpuscles, and a granular exudate. The alveolar structure became obscured. Finally, with the continued administration of the toxin, the affected areas became transformed into connective tissue.

HEART (TALQUIST). About fifty hearts were examined by transverse and longitudinal sections, stained principally by hæmotoxylin and eosin, and by Van Gieson's method. No fresh examinations were made.

By the injection of bouillon cultures of the streptococcus directly into the heart muscle pericarditis resulted in nearly all cases. Most animals died in two to three days. In the heart muscle small abscesses developed in some cases. In other cases there were small foci made up of necrotic muscle fibres and much round-cell infiltration. In these foci were numerous cocci. Vascular infiltration was marked and small hemorrhages frequent. Later the formation of fibroblasts was observed. Simple parenchymatous changes were not common. In a rabbit which recovered, and was killed after a month and a half, repair with abundant formation of connective tissue was observed. The foci in the heart muscle were often due apparently to direct extension from the pericarditis, but in many cases isolated foci were found in deeper portions of the wall and in the papillary muscles.

After injection of bouillon cultures into the ear-vein changes in the heart muscle were quite constant. After twenty-four hours cocci could be seen in large numbers between the muscle fibres, and this was soon followed by destruction of the muscle fibres and round-cell infiltration. Marked vascular hyperæmia was common. In some cases hyaline degeneration of muscle fibres and proliferation of muscle nuclei were seen. In later stages diffuse interstitial changes occurred. There was slight evidence of fatty degeneration.

Subcutaneous and intraperitoneal injections, and injections into the sciatic nerve, produced changes similar to the above. In several of the cases acute pericarditis and endocarditis occurred.

After the injections of the toxins into the ear-veins, even in cases with increase of temperature and loss of weight, the heart muscle frequently remained normal. Changes which did occur were parenchymatous in nature, consisting in granular changes in the fibres and in fatty, hyaline, and waxy degeneration. In later stages interstitial changes were sometimes seen. The left ventricle and intraventricular septum were the parts most frequently affected.

KIDNEYS. VON BONSDORFF presents experimental investigations on the elimination of streptococci by the kidneys. He injected twenty-four-hour bouillon cultures into the ear-vein or peritoneal cavity of rabbits, and endeavored to find how soon the organisms were present in the urine, and if any constant relation existed between the appearance of cocci in the urine and structural changes in the kidney.

The appearance of cocci in the urine was not constant. The shortest time was nine and one-half hours after injection. In five cases, with a fatal result after a period varying from seven to fifty-five days, the urine was sterile throughout. In a few cases the cocci were present for a few days and then disappeared. As a rule the colonies increased in number with the progress of the case.

Microscopical examination showed in some cases, in the outer parts of the cortex, slight desquamation of epithelium, with nuclei somewhat contracted. In older cases there occurred a slight fatty degeneration, especially in the epithelium of the loops in the upper part of the medulla. Before the fifth day, and in control sections, fat was never found here. Cellular infiltration and frank nephritis were not observed.

In those cases in which streptococci were found in the kidney by culture they were usually present in sections as well. They were found most often in the tufts, less often in the intertubular capillaries, and only very rarely within the tubules; not at all in the capsular space.

These results are too few and incomplete to settle the question as to whether bacteria can pass through normal kidneys. In the first few hours after injection there is no elimination of bacteria. This points to certain antecedent changes in the kidney.

PERITONEAL CAVITY (WALLGREN). The same virulent organism used in the preceding experiments was injected into the peritoneal cavity, and the changes produced were followed by aspirating fluid from the cavity at various intervals of time. In most of the experiments the animals died from a general infection.

The writer sums up his results as follows:

Virulent streptococci, injected even in rather small quantities into the peritoneal cavities of rabbits, can produce a fatal peritoneal infection even when the animal is not particularly susceptible.

If virulent streptococci are injected in doses below a certain minimum the peritoneum can get rid of the organism, but the abdominal wall usually becomes infected around the site of inoculation.

Streptococci of slight virulence do not develop in the peritoneal cavities of rabbits, even if present in large quantities, provided the fluid injected with them is small in amount.

The peritoneal cavity is protected chiefly by its great power of absorption, by the activity of the leucocytes in and immigrating into it, and possibly also by the function of the endothelial cells of the peritoneum.

The leucocytes aid in the battle against the streptococci by phagocytosis, by their products of degeneration, and, perhaps, also, by their secretions.

In experiments with virulent streptococci, phagocytosis occurs at the beginning of infection, is almost lacking in the following stage, when the streptococci have acquired the power to keep the leucocytes at a distance, but can return again later, apparently when the leucocytes begin to break down more rapidly.

In experiments with streptococci of slight virulence, phagocytosis persists uninterruptedly the whole time, so long as streptococcci are present in the peritoneal cavity.

The streptococci can have a disturbing effect on the leucocytes. This is shown by the alteration and disappearance of the neutrophilic granules of the polymorphonuclear leucocytes, a process most marked in the granules around streptococci included within the cells.

So long as streptococci are demonstrable in the peritoneal cavity, as well as for one to two days after their disappearance, the majority of the cells present are polymorphonuclear leucocytes. Later there is for some time a leucocytosis which is chiefly mononuclear.

[The above work is ambitious, and is illustrated with many beautiful plates, but is not complete. The blood, spleen, and bone-marrow, for instance, were not studied. The most interesting portion is that on the lesions produced in the peripheal nerves and the central nervous system. The chief criticism on the work is that it is not wholly satisfactory in the study of the finer histological changes in the various organs.—Ed.]

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